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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,470	09/23/2003	Rajeev A. Jain	029318-0972	9048

31049 7590 03/11/2008

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
03/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/667,470	JAIN ET AL.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-51, 54-107 and 110-111* is/are pending in the application.

4a) Of the above claim(s) *54-86,110 and 111* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-51 and 87-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's filing of amendment/remarks on 12/13/07. By the amendment, claims 27-28, 50, 87 and 106 have been amended; and claims 52-53 and 108-109 have been cancelled. Claims 27-51 and 87-107 are currently pending for prosecution on the merits of the case.

2. Applicant's amendment changing the scope of the invention by excluding ketoprofen or naproxen necessitates a new ground of rejection in this Office Action.

3. Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

4. With respect to the rejection of claims 27-53 and 87-109 under the judicially created doctrine of double patenting, the examiner maintains the rejection of record since no Terminal Disclaimer is filed and approved in our PTO record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 27-51 and 87-107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims in this application introduce new negative limitations, namely "wherein the active agent is not ketoprofen or naproxen". The examiner determines that when all evidences in the original disclosure are considered and carefully reviewed, the newly amended claims fail to find support in the original specification.

There is no express statement about the negative limitation that can be found in the specification. Thus, the exclusion of said elements implies the inclusion of all other elements not expressly excluded, clearly illustrating that such negative limitations do, in fact, introduce new matter. The negative limitation recited in the present claims, which did not appear in the specification filed, introduces new concepts and violate the description requirement of the first paragraph of 35 USC 112.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 27-34, 37-47, 50-51, 87-93 and 96-107 are rejected under 35 U.S.C. 102(b) as being anticipated by Eickhoff et al. (USP 5518738).

Eickhoff discloses a rapidly-acting solid oral dose form pharmaceutical composition comprising nanoprticulate (crystallyine) NSAIDs, for example etodolac, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethain, ketoprofen, meclofenamate, mefenamic acid, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, sunlindac, tenoxicam, tiaprofenic acid, tolmetin, etc…, dispersed in mixtures of hydroscopic sugar (i.e., mannitol), polyvinylpyrrolidone and sodium lauryl sulfate, wherein the polyvinylpyrrolidone surface modifier mixed with the hygroscopic sugar and sodium lauryl sulfate is adsorbed on the surface of the NSAIDs (abstract; column 2, lines 41-50; column line 59 through column 3, line 32; column 3, lines 36-48; column 5, lines 45-52; claims 1-10 and 15; claims 1-10, particularly claim 4), wherein the average particle size of the NSAIDs is less than about 1000 nm, preferably less than 300nm (column 3, lines 49-59); the concentration of the NSAID is in range from about 0.1 to 60% (column 4, lines 16-21; the concentration of polyvinylpyrrolidone is in range from about 0.1 to about 90% (column 4, lines 21-24 and column 5, lines 42-44); the concentration of the hydrogroscopic sugar (i.e., mannitol) in range of from 10 to 75% (column 5, lines 53-54); and the concentration of the sodium lauryl sulfate is in range of from 0.1 to 10% (column 5, lines 55-57); and the dispersion is sprayed dried to a fine powder in a fluidized bed coater (Examples). As the specific embodiment of the claimed invention, Eickhoff discloses examples of oral solid dosage form comprising nanoparticulate naproxen (approximately 200 nm) having mixtures of polyvinylpyrrolidone, mannitol and sodium lauryl sulfate dispersant adsorbed on the

surface (Examples 1 and 2). Eickhoff also discloses a method of treating a mammal comprising administering said composition (see claims 11-14).

With respect to "at least one surface stabilizer substantially completely disintergrates or dissolves upon contact with saliva is less than about 3 minutes" in claims 27 and 87, "substantially completely disintegrates or dissolves upon contact with saliva in a time period selected from the group consisting of less than about 2 minutes…" in claim 28, although Eickhoff is silent about such characteristic or property of the surface stabilizer or the formulation, such property or characteristic deems to be inherent to the referenced composition since the essential components of Eickhoff are identical to the instant composition (that is an oral solid dose rapidly disintegrating or acting nanoprticulate NSAID having an average particle size of less than 1000nm and water-dispersible excipient and/or a surface stabilizer (i.e., polyvinylpyrrolidone, mannitol and sodium lauryl sulfate)). Thus, Eickhoff anticipates the instant invention.

With respect to "said excipient is selected from the group consisting of a direct compression material and a non-direct compression material" in claims 45 and 104, such property or characteristic deems to be inherent to the referenced excipients such as mannitol. Thus, Eickhoff anticipates the instant invention.

7. Claims 27-48, 50-51 and 87-107 are rejected under 35 U.S.C. 102(e) as being anticipated by Kerkhof et al. (WO 01/45674 A1).

Kerkhof disclose nanoparticle compositions comprising a nonsoluble drug (i.e., indomethacin, naproxen and ketoprofen) and water-dispersible excipient (i.e., polyvinyl pyrrolidone, mannitol, lactose, carbonates, bicarbonates, etc…), and/or surface stabilizer such as

surfactant, wherein said composition is made by fluid bed granulation and spray-drying method where a suitable excipient, such as spray-dried lactose, is fluidized by an upward gas stream; and wherein one part by weight of an active ingredient is combined with about 2.5 to about 50 parts, preferably about 2.5 to about 20 parts of an excipient (abstract; page 10, lines 1-12; page 10, line 25 through page 11, line 9; page 11, lines 10-27; page 15, lines 1-18; page 8, lines 11-16 and 25-27; page 15, lines 1-17; page 12, line 29 thru page 13, line 6; Claims, particularly claims 1-2, 7, and 19). According to Kerkhof, the nanoparticle can have a mean particle size between 50-1000 nm (Claim 2 and page 7, lines 20-23). The composition can be fashioned into tablets, capsules or syrups (page 14, lines, 12-15). According to Kerkhof, the method of preparing a nanoparticle composition can comprise spraying a solution of a poorly soluble drug and a solvent into a bed of carrier particles (claim 1). The solution may further comprise a surface modifier, such as a surfactant (claims 1, 18, 19). The nanoparticle composition can have a mean particle size of around between 50-1000nm (claim 2 and page 7,lines 20-23). Kerkhof also disclose a method of administering a nanoparticle composition comprising a surface modifier, such as a surfactant, and a drug to a human (page 14, lines 16-27). Prior to administration, the composition may be formulated into a tablet (page 14, lines 12-15).

With respect to "at least one surface stabilizer substantially completely disintergrates or dissolves upon contact with saliva is less than about 3 minutes" in claims 27 and 87, "substantially completely disintegrates or dissolves upon contact with saliva in a time period selected from the group consisting of less than about 2 minutes…" in claim 28, although Kerkhof is silent about such characteristic or property of the surface stabilizer or the formulation, such property or characteristic deems to be inherent to the referenced composition since the essential

components of Kerkhof are identical to the instant composition (that is an oral solid dose rapidly disintegrating or acting nanoprticulate NSAID having an average particle size of less than 1000nm and water-dispersible excipient and/or a surface stabilizer (i.e., polyvinylpyrrolidone, mannitol and sodium lauryl sulfate)). Thus, Eickhoff anticipates the instant invention.

With respect to "said excipient is selected from the group consisting of a direct compression material and a non-direct compression material" in claims 45 and 104, such property or characteristic deems to be inherent to the referenced excipients such as mannitol. Thus, Kerkhof anticipates the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eickhoff et al. (USP 5518738) or Kerkhof et al. (WO 01/45674 A1), and further in view of applicant's admitted prior art of record (page 3, lines 13-22).

The teaching of Eickhoff or Kerkhof has been discussed in above 35 USC 102(b) or (e) rejection.

Applicant's admitted prior art of record discloses the routine knowledge in preparing pharmaceutical oral dosage forms via free-drying techniques.

The teaching of either Eickhoff or Kerhof differs from the claimed invention in the lyophilization (freeze drying) of said composition. However, one having ordinary skill in the art would have been motivated to modify the teaching of either Eichhoff or Kerhof to improve the pharmacological activity of the poorly soluble active agent. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 27-51 and 87-107 are rejected under the judicially created doctrine of double patenting over claims 1-24 and 51-70 of USP 6316029.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and the patent are directed to a oral solid dose rapidly disintegrating nanoparticulate formulation comprising water-soluble or water-dispersible excipient and a poorly soluble active agent less than about 200 nm prior to inclusion in the dosage forms and at least one surface stabilizer.

10. Claims 27-51 and 87-107 are rejected under the judicially created doctrine of double patenting over claims 1-16 and 21 of USP 6165506, further in view of the applicant's admitted prior art of record (page 3, lines 13-22)..

Although the conflicting claims are not identical, they are not patentably distinct from each other because Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and the patent are directed to a oral solid dose nanoparticulate formulation comprising water-soluble or water-dispersible excipient

and a poorly soluble active agent less than about 200 nm prior to inclusion in the dosage forms and at least one surface stabilizer.

Although USP'506 is silent about the characteristic of said composition having "rapidly disintegrating", such property or characteristic deems to be inherent to the referenced composition since the essential components of USP'506 are identical to the instant composition. Thus, USP'506 anticipates the instant invention.

With respect to "lyophilized" in claim 49, as discussed above, the applicant's admitted prior art of record makes obvious the preparing said composition containing said poorly soluble drug in lyopholization method is well within the skill of the artisan.

In looking in continuity data, it is noted that applicant has numerous issued patent and pending applications encompassing the same or similar subject matter of the instant application. Applicant should review all subject matter considered the same or similar, and submit the appropriate Terminal Disclaimer(s). For example, 10/444066, 11/274069, 11/592264 and 09/337675 are drawn to same or similar subject matter(s).

Response to Arguments

11. Applicant's arguments filed 12/13/07 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that the "essential components" of Eickhoff are not identical to the claimed composition, as the claimed composition, as amended, excludes ketoprofen and naproxen

This argument is not found persuasive. Unlike the applicant's argument, Eickhoff discloses other NSAIDs (having selective or non-selective COX-2 inhibiting activity) such as etodolac, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethain, meclofenamate, mefenamic acid, meloxicam, nabumetone, oxaprozin, piroxicam, sunlindac, tenoxicam, tiaprofenic acid, tolmetin, etc…. Thus, the reference anticipates the claimed invention.

In response to the applicant's argument that Kerkhof fails to describe the instant required "rapid disintergration" characteristic of said composition, the examiner recognizes that the recitation of functional property or characteristic of said composition is not limited to the interpretation of composition claims. Thus, the reference anticipates the claimed invention.

In response to the applicant's argument that ", Kerkhof does nothing more than provide a laundry list of choices and combination of the nonsoluble drug ingredients, carrier excipients and surface stabilizer", the examiner recognizes that "indomethacin, naproxen and ketorpfen" are disclosed as specific examples of the appropriate drug for the formulation. "indomethacin, naproxen and ketoprofen" are drugs among about 40 of agents that are listed as most suitable for the invention (see page 9, line 28 through page 10, line 12). Thus, one of ordinary skill in the art would "at once envisage" the claimed compounds and arrived at the claimed invention.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching,

suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, .

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. No Claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614